

Amendments to the Specification:

Please insert the sequence listing being filed concurrently herewith into the specification.

Please replace paragraph [0034] with the following new paragraph:

[0034] Fig. 1. Organization of the Human PEDF-R1 cDNA. **A.** The ORF is indicated by an open box, the predicted transmembrane (TM) domains by gray boxes (amino acid residues 7-24, 43-63, 140-159, and 325-347) and N-glycosylation sites by ticks at the top (amino acid residues 9, 39, 209 and 425). The hatched box shows the PEDF binding region p12 (amino acid residues 250-383). **B.** Hydrophobicity plot of the derived amino acid sequence of R1. **C.** Diagram showing a model for R1 topology. TM positions with preferred orientations were predicted using TMpred software. **D.** Amino acid sequence derived from human R1 cDNA (SEQ ID NO:3) and its alignment to adiponutrin (SEQ ID NO:27). Non conserved amino acids sequence is shown for the adiponutrin. A patatin-like region is in ***bold italic*** (amino acid residues 7-180) and TM domains are indicated by open boxes. **E.** Regions of R1 (p12 and C-terminal region) (SEQ ID NO:28) showing similarity with human collagen I (alpha chain). Sequences were aligned using SIM-LALNVIEW software and similarities above a threshold of 25% were considered. The range of identity between p12 regions (253-293) and several areas of human collagen I (alpha chain) (SEQ ID NO:29) is 25-71.4%. The range of identity between a C-terminal regions of R1 (450-504) and several areas of human collagen I (alpha chain) is 25-66.7%. Proline (red) rich regions, typical of collagen chain, are shown. This shows that R1 has similarity to human collagen I in the PEDF binding region (p12) and C-end region. We have shown that PEDF has binding affinity for collagen I. before (Meyer et al., JBC, 277: 45400-7, 2002). This is of interest because it may represent the molecular basis for the binding affinity of R1 for PEDF. **F.** Alignment of partial sequences around conserved residues of R1 (SEQ ID NO:30), patatin B2 (SEQ ID NO:32) and cytoplasmic cPLA2 (SEQ ID NO:32). Active site residues of cPLA2: Ser228, Asp549, of patatin B2 Ser54 and Asp192. The homologous patatin phospholipase A (PLA) active residues of human R1 (SEQ ID NO:33) correspond to Ser47 (S47) and Asp166 (D166). The sites in Patatin B2 (SEQ ID NO:34) and cPLA2 (SEQ ID NO:35) have been obtained from crystallographic and mutational studies of these proteins (Hirschberg et al.,

Eur J Biochem, **268**: 5037-5044, 2001). X-ray crystallographic data clearly revealed that patatin possessed a Ser-Asp catalytic dyad and an active site similar to that observed in the catalytic domain of human cytosolic cPLA2 (Rydel *et al.*, *Biochemistry*, **42**: 6696-6708, 2003).

Please replace paragraph [0052] with the following new paragraph:

[0052] **Fig. 19.** Figure 19 provides the amino acid alignment of the mouse (Accession number BAC27476.1; SEQ ID NO:14), rat (Accession number XP_341961.1; SEQ ID NO:17) and human (Accession number AAH17280.1; SEQ ID NO:3) PEDF-R protein.

Please replace paragraph [0053] with the following new paragraph:

[0053] **Fig. 20.** Figure 20 provides the nucleic acid alignment of the mouse (Accession number AK031609.1; chromosome 7; SEQ ID NO:12), rat (Accession number XM_341960.1; chromosome 1; SEQ ID NO:15) and human (Accession number BC017280.1; chromosome 11; SEQ ID NO:1) PEDF-R cDNA.

Please replace paragraph [0246] with the following new paragraph:

[0246] With respect to the parental immunoglobulin, a useful joining point is just upstream of the cysteines of the hinge that form the disulfide bonds between the two heavy chains. In a frequently used design, the codon for the C-terminal residue of the PEDF-R part of the molecule is placed directly upstream of the codons for the sequence DKTHTCPPCP (SEQ ID NO:24) of the IgG1 hinge region.

Please replace paragraph [0392] with the following new paragraph:

[0392] Primers for screening the expression of p12 sequence were 12-forward, 5' AAC CCC TTG CTG GCG TTG C 3' (SEQ ID NO:25); and 12-reverse, 5' CCC GTC TGC TCC TTC ATC C 3' (SEQ ID NO:26). Templates were R1 cDNA, cDNAs prepared from human retina, human RPE, ARPE-19 and human TERT in PCR SuperMix reactions following instructions by manufacturer (Invitrogen).

Please replace paragraph [0393] with the following new paragraph:

[0393] Oligonucleotide primers were designed to flank the DNA fragment containing the PEDF interacting region obtained from the yeast-2 hybrid. The forward primer #1 was 5'Cacc aTG CAG CGG AAC GGC CTC CTG AAC C 3' (SEQ ID NO:6) (Cacc + gene specific). Two reverse primers were: #2, 5'Cta GTT CCT CTT GGC GCG CAT CAC C 3' (SEQ ID NO:7) (gene specific+ stop) and #3, 5'GTT CCT CTT GGC GCG CAT CAC C 3' (SEQ ID NO:8) (gene specific). PCR reactions with primers #1 and 2 were set with R1 as template to amplify p12 with a ATG and Stop codon. PCR reactions with primers #1 and 3 were set with R1 as template to amplify p12 with only the ATG codon. The PCR products were inserted into entry vectors pENTR-TOPO-D and pENTR-TOPO-SD, respectively by the TOPO reactions (Invitrogen). The p12 inserts were recombined into expression vectors pEXP-DEST-1 and pEXP-DEST-2, respectively, using LR recombinase (Invitrogen). The resulting plasmids were termed pEXP-12N and pEXP-12C and contained p12 sequences with a fusion His Tag at the N-terminus and C-terminus, respectively. The derived recombinant polypeptide from the pEXP-12N was termed p12N, and the one from pEXP-12C was termed p12C.